

FIGURE 1

BEST AVAILABLE COPY

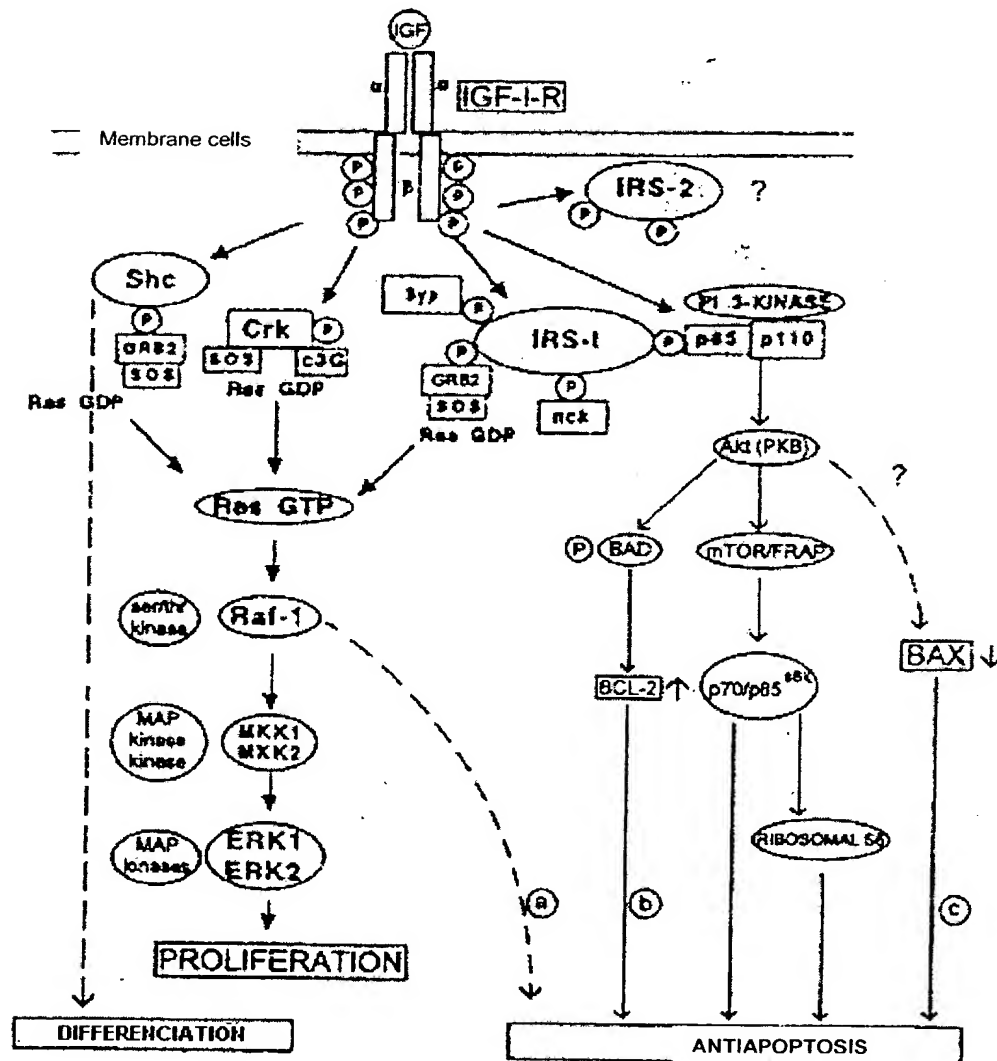


FIGURE 2

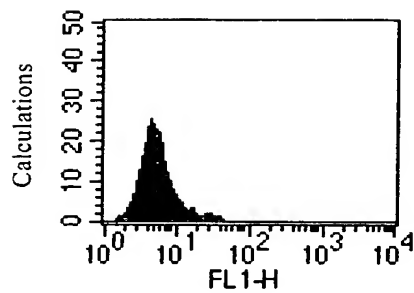


FIGURE 3A

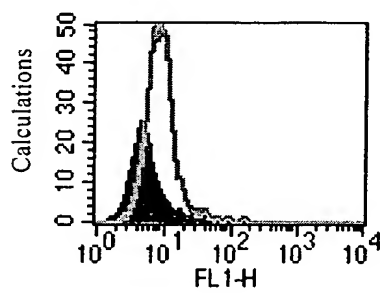


FIGURE 3B

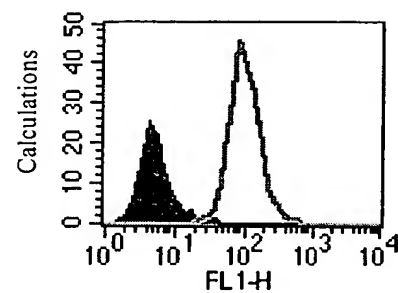
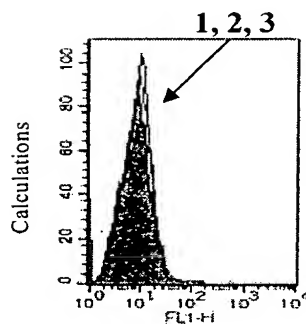
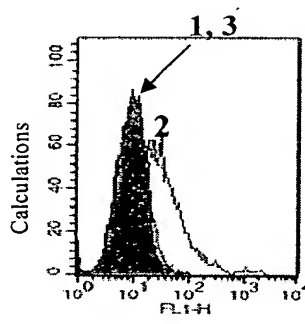


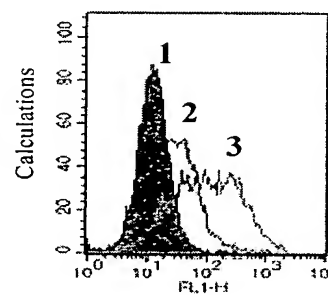
FIGURE 3C



Nontransfected cells



IGF-IR+ cells



IR+ cells

FIGURE 4A

FIGURE 4B

FIGURE 4C

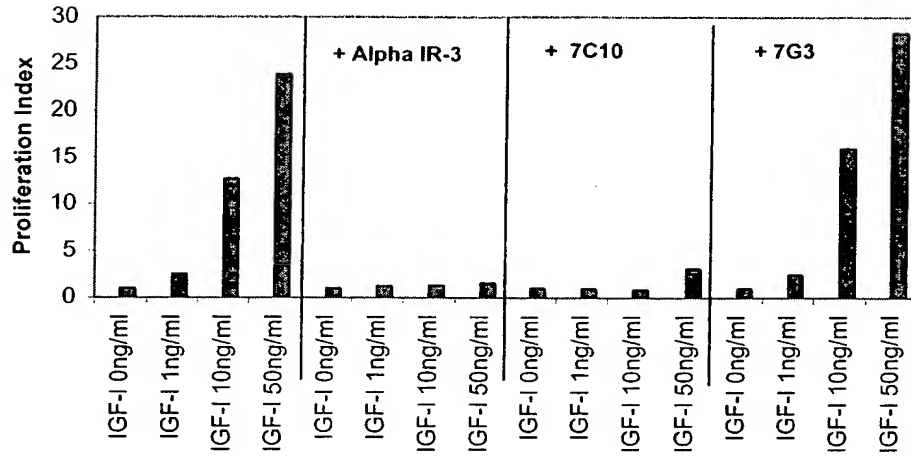


FIGURE 5

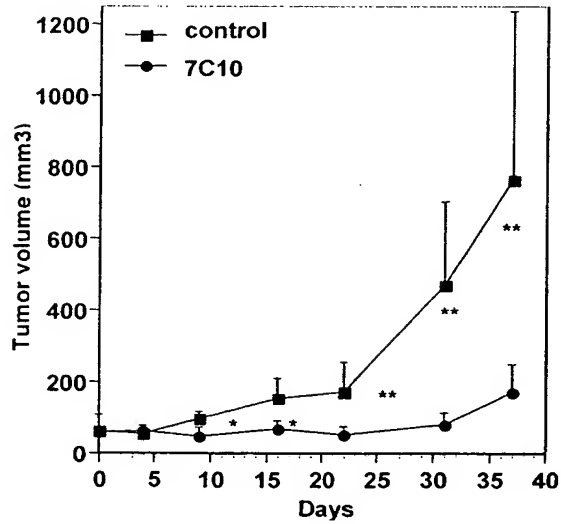


FIGURE 6A

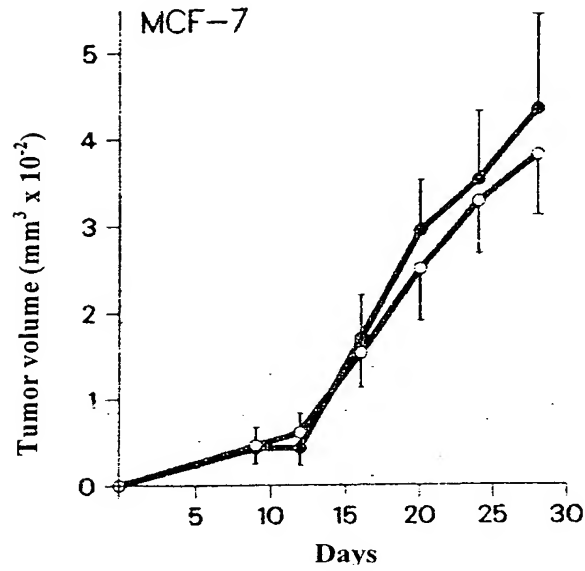


FIGURE 6B

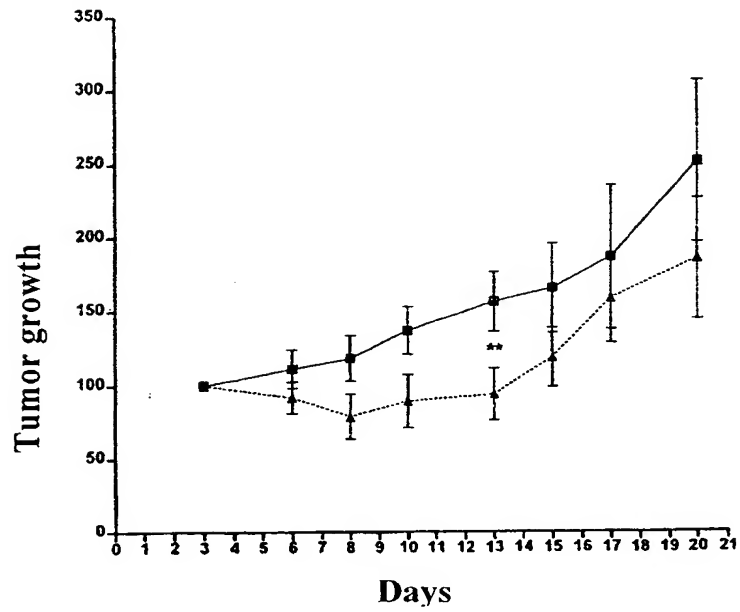


FIGURE 6C

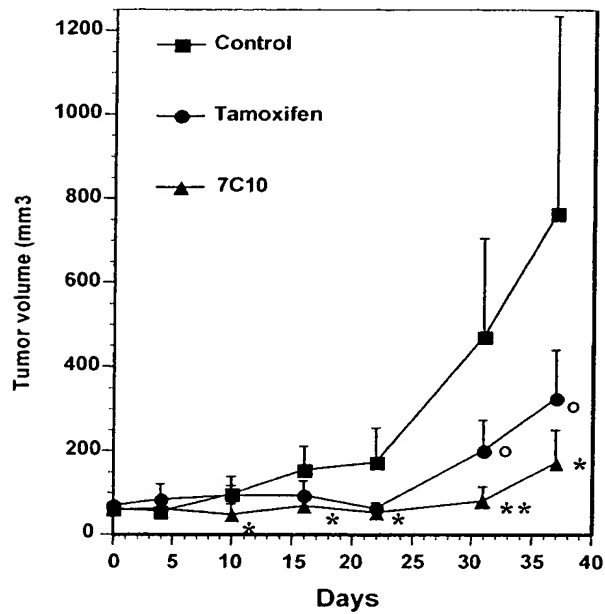


FIGURE 7

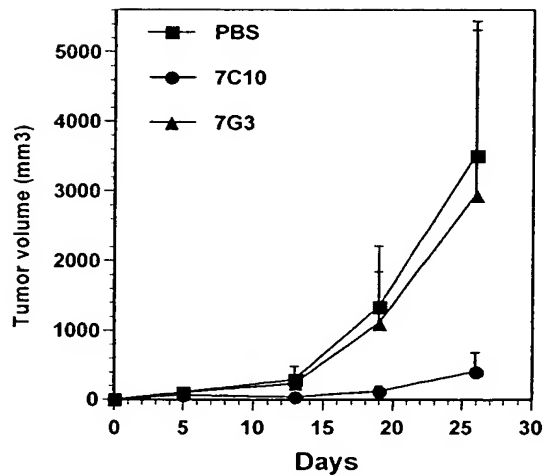


FIGURE 8A

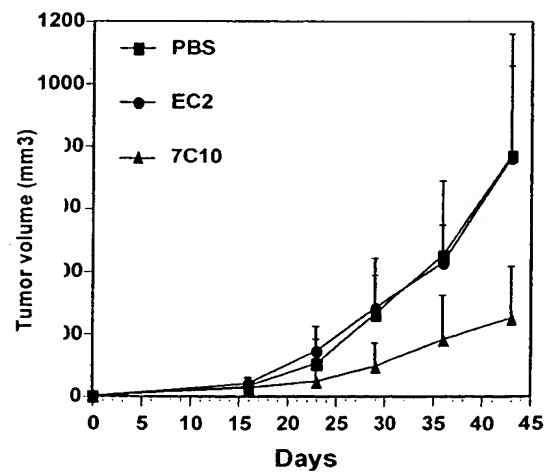


FIGURE 8B

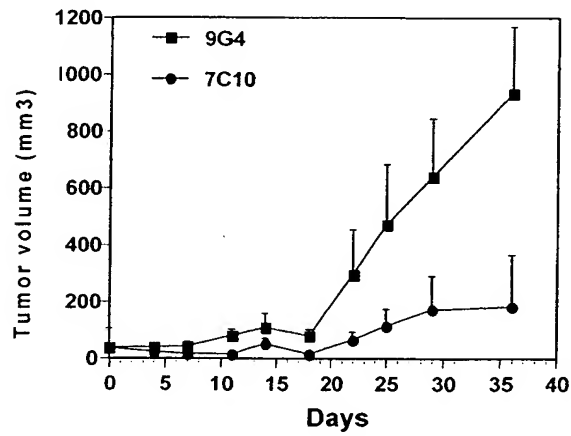


FIGURE 8C

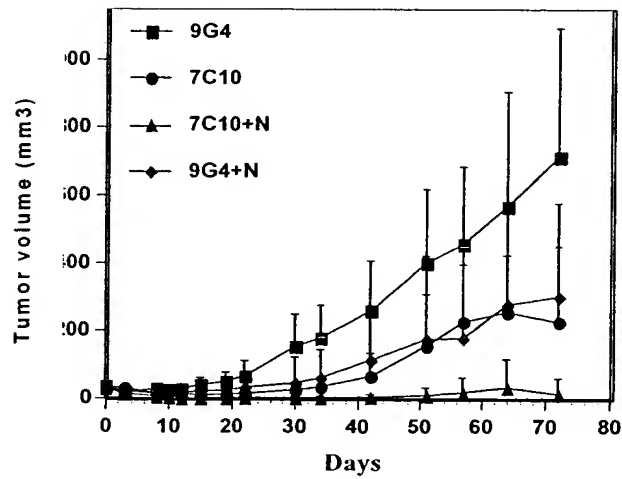


FIGURE 9

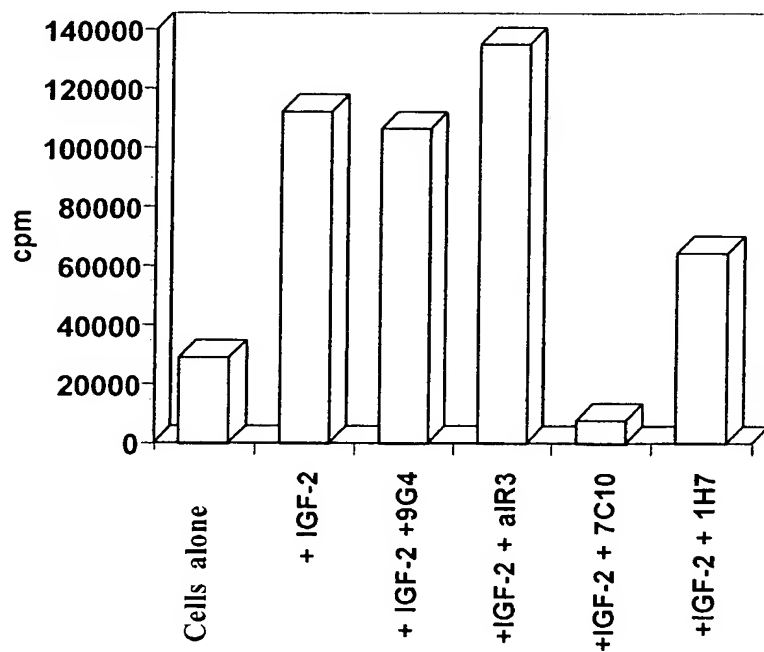


FIGURE 10

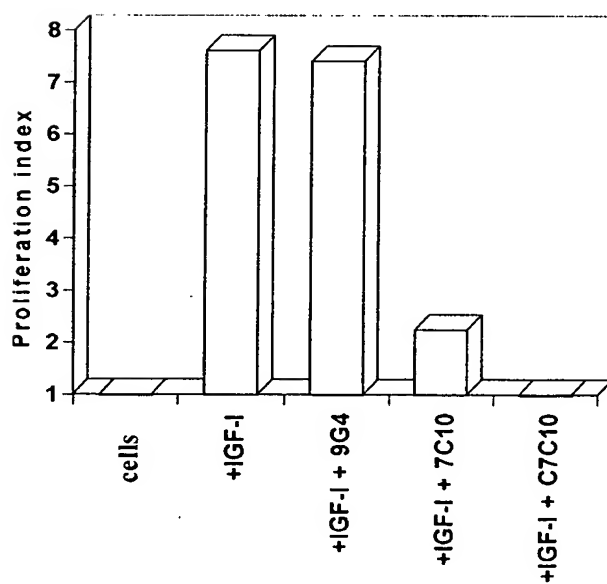


FIGURE 11



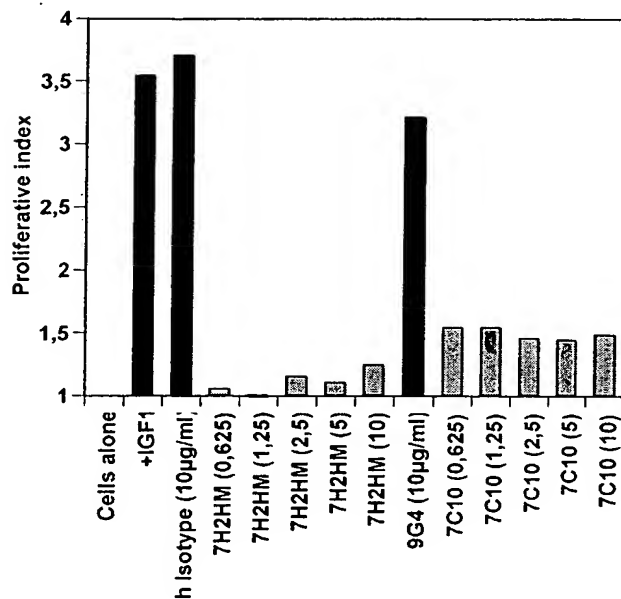


FIGURE 12

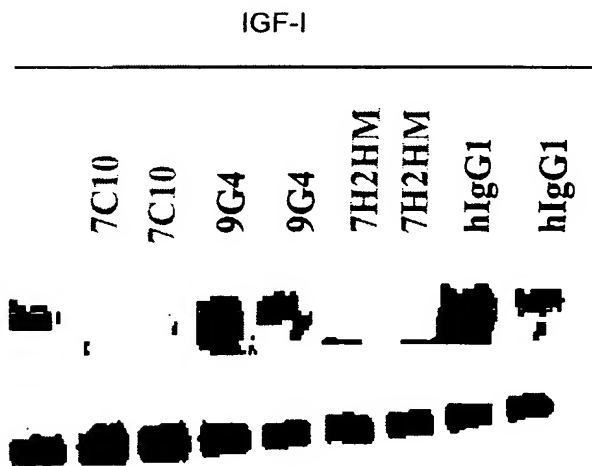


FIGURE 13

```

ATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGGATTCTGCTTCCAGAAGTGAT
1  -----+-----+-----+-----+-----+-----+ 60
TACTTCAACGGACAATCCGACAACCACGACTACAAGACCTAAGGACGAAGGTCTTCACTA
ATGAAGTTGCCTGTTAGGCTGTTGGTGCT
      oligo MKV-1      L M F W I P A S R S D -
                        3' end      leader peptide
GTTTTGATGACCCAAATTCCTACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATC
61  -----+-----+-----+-----+-----+-----+ 120
CAAACACTACTGGGTTTAAGGTGAGAGGGACGGACAGTCAGAACCTCTAGTTCGGAGGTAG

V L M T Q I P L S L P V S L G D Q A S I -

TCTTGCAAGATCTAGTCAGAGCATTGTACATAGTAATGGAAACACCTATTTACAATGGTAC
121 -----+-----+-----+-----+-----+-----+ 180
AGAACGTCTAGATCAGTCTCGTAACATGTATCATTACCTTTGTGGATAAATGTTACCATG

S C R S S Q S I V H S N G N T Y L Q W Y -
                        CDR 1
CTGCAGAAACCAGGTCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGACTTTAT
181 -----+-----+-----+-----+-----+-----+ 240
GACGTCTTTGGTCCAGTCAGAGGTTTCGAGGACTAGATGTTTCAAAGGTTGGCTGAAATA

L Q K P G Q S P K L L I Y K V S N R L Y -
                        CDR 2
GGGGTCCCAGACAGGTTTCAGTGGCAGTGGATCAGGGACAGATTTCACTCAAGATCAGC
241 -----+-----+-----+-----+-----+-----+ 300
CCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAGTCG

G V P D R F S G S G S G T D F T L K I S -

AGCGTGGAGGCTGAGGATCTGGGAGTTTATTACTGCTTTCAAGGTTACATGTTCCGTGG
301 -----+-----+-----+-----+-----+-----+ 360
TCGCACCTCCGACTCCTAGACCCTCAAATAATGACGAAAGTTCCAAGGTACAAGGCACC

S V E A E D L G V Y Y C F Q G S H V P W -
                        CDR 3
GG
ACGTTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCTGATGCTGCACCAACTGTATCC
361 -----+-----+-----+-----+-----+-----+ 420
TGCAAGCCACCTCCGTGGTTCGACCTTTAGTTTGCCCGACTACGACGTGGTTGACATAGG

T F G G G T K L E I K

      MKC oligo
      TAGAAGGGTGGTAGGTCA
      ATCTTCCCACCATCCAGT
421 -----+-----+-----+-----+-----+ 438
      TAGAAGGGTGGTAGGTCA
  
```

FIGURE 14

GGTAGACAGATAGGTGAC

**FIGURE 15**

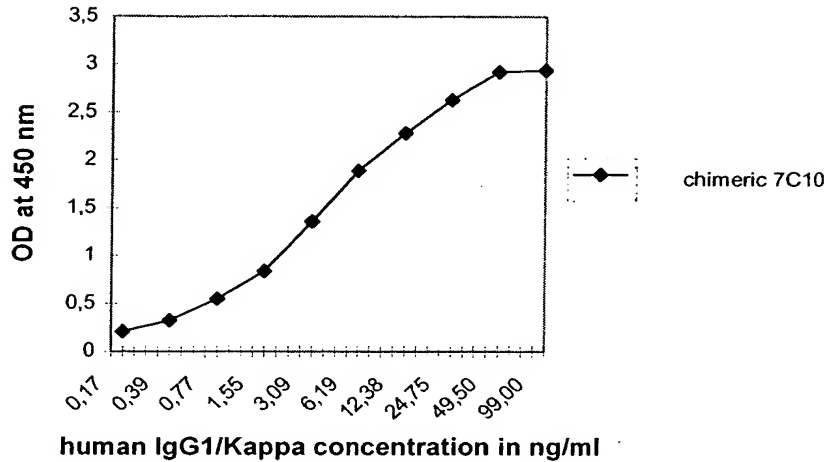


FIGURE 16

	3	7		<b>CDR 1</b>
7C10 VL mouse	DVL	MTQIPLSLPVSLGDQASISC	<b>RSSQSIVHSNGNTYLQ</b>	
DRB1-4.3	.....	T.....	.....	<b>E</b>
C94-5B11' CL	.....	T.....	.....	<b>E</b>
Kabat sgII mouse	..V..	..T..	.....L.....	<b>E</b>

		<b>CDR 2</b>
7C10 VL mouse	WYLQKPGQSPKLLIY	<b>KVSNRLY</b> GVPDRFSGSGSGTDFTL
DRB1-4.3	.....	<b>FS</b> .....
C94-5B11' CL	.....	<b>FS</b> .....
Kabat sgII mouse	.....	<b>FS</b> .....

	77		<b>CDR 3</b>
7C10 VL mouse	KISSVEAEDLGVIYC	<b>FQGSHPWT</b>	FGGGTKLEIK
DRB1-4.3	...R.....	<b>F</b> ..S...	D..
C94-5B11' CL	...R.....	.....	.....
Kabat sgII mouse	...R.....	<b>T</b> ...Y.	.....

FIGURE 17

**CDR 1**

7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>
GM607	.IV...S.....TP.EP.....	.....LL....YN..D
DPK15/A19	.IV...S.....TP.EP.....	.....LL....YN..D
Kabat sgII hu	.IV...S.....TP.EP.....	.....LL..D.XX..X

**CDR 2**

7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTLK
GM607	.....Q....	LG...AS	.....
DPK15/A19	.....Q....	LG...AS	.....
Kabat sgII hu	.....Q....	L...AS	.....

**CDR 3**

7C10 VL mouse	ISSVEAEDLGVIYC	<u>FQGSHPWT</u>	FGGGTKLEIK
GM607	..R.....V.....	M.ALQT.Q.	..Q...V...
DPK15/A19	..R.....V.....	M.ALQT.	
Kabat sgII hu	..R.....V.....	M.ALQX.R.	..Q...V...

FIGURE 18

**CDR 1**

7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>
GM 607	.IV...S.....TP.EP.....	.....LL....YN..D
7C10 VL Humanized 1	..V...S.....TP.EP.....	.....
7C10 VL Humanized 2	.IV...S.....TP.EP.....	.....

**CDR 2**

7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTL
GM 607	.....Q....	LG...AS	.....
7C10 VL Humanized 1	.....Q....		
7C10 VL Humanized 2	.....Q....		

**CDR 3**

7C10 VL mouse	KISSVEAEDLGVIYC	<u>FQGSHPWT</u>	FGGGTKLEIK
GM 607	...R.....V.....	M.ALQT.Q.	..Q...V...
7C10 VL Humanized 1	...R.....V.....		..Q...V...
7C10 VL Humanized 2	...R.....V.....		..Q...V...

FIGURE 19

MluI  
 |  
 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG  
 1 -----+-----+-----+-----+-----+ 60  
 CAGTCTTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

M K L P V R L L V L M F W -  
 Peptide leader  
 TTTCTGCTTCCAGCAGTGATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCCGTCACC  
 61 -----+-----+-----+-----+-----+ 120  
 AAAGGACGAAGGTCGTCAC TACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG

2  
 F P A S S S D V V M T Q S P L S L P V T -  
 CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA  
 121 -----+-----+-----+-----+-----+ 180  
 GGACCTCTCGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT

CDR 1  
 P G E P A S I S C R S S Q S I V H S N G -  
 KpnI  
 |  
 AACACCTATTTGCAATGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT  
 181 -----+-----+-----+-----+-----+ 240  
 TTGTGGATAAACGTTACCATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA

N T Y L Q W Y L Q K P G Q S P Q L L I Y -  
 AAAGTTTCTAATCGGCTTTATGGGGTCCCTGACAGGTTTCAGTGGCAGTGGATCAGGCACA  
 241 -----+-----+-----+-----+-----+ 300  
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT

CDR 2  
 K V S N R L Y G V P D R F S G S G S G T -  
 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCTTT  
 301 -----+-----+-----+-----+-----+ 360  
 CTAAAATGTGACTTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA

D F T L K I S R V E A E D V G V Y Y C F -  
 CAAGGTTACATGTTCCGTGGACGTTCCGGCCAAGGGACCAAGGTGGAATCAAACGTGAG  
 361 -----+-----+-----+-----+-----+ 420  
 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTTCCTGGTTCCACCTTTAGTTTGCACTC

CDR 3  
Q G S H V P W T F G Q G T K V E I K  
 BamHI  
 |  
 TGGATCCTCTGCG  
 421 -----+-----+-----+ 433  
 ACCTAGGAGACGC

FIGURE 20

MluI  
 |  
 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG  
 1 -----+-----+-----+-----+-----+ 60  
 CAGTCTTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

M K L P V R L L V L M F W -  
 Leader peptide

TTTCCTGCTTCCAGCAGTGATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC  
 61 -----+-----+-----+-----+-----+ 120  
 AAAGGACGAAGGTCGTCACTACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG

2  
 F P A S S S D I V M T Q S P L S L P V T -

CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA  
 121 -----+-----+-----+-----+-----+ 180  
 GGACCTCTCGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT

CDR 1

P G E P A S I S C R S S Q S I V H S N G -

KpnI  
 |

AACACCTATTTGCAATGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT  
 181 -----+-----+-----+-----+-----+ 240  
 TTGTGGATAAACGTTACCATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA

N T Y L Q W Y L Q K P G Q S P Q L L I Y -

AAAGTTTCTAATCGGCTTTATGGGGTCCCTGACAGGTTTCAGTGGCAGTGGATCAGGCACA  
 241 -----+-----+-----+-----+-----+ 300  
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT

CDR 2

K V S N R L Y G V P D R F S G S G S G T -

GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCTTT  
 301 -----+-----+-----+-----+-----+ 360  
 CTAAATGTGACTTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA

D F T L K I S R V E A E D V G V Y Y C F -

CAAGGTTACATGTTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAATCAAACGTGAG  
 361 -----+-----+-----+-----+-----+ 420  
 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTTCCTGGTTCCACCTTTAGTTTGCACTC

CDR 3

Q G S H V P W T F G Q G T K V E I K

BamHI  
 |  
 TGGATCCTCTGCG  
 421 -----+----- 433  
 ACCTAGGAGACGC

FIGURE 21

	17	27	<b>CDR 1</b>
<b>7C10 VH</b>	DVQLQESGPGGLVKPSQSLSLTCSVTGYSIT		<b>GGYLWN</b> WIRQ
<b>AN03' CL</b>	.....		<b>S..Y..</b> ....
Kabat sgI(A)	<u>E</u> ..... <u>S</u> ..... <u>T</u> ..... <u>D</u> ...		<b>S..WN.</b> ...

	<b>CDR 2</b>
<b>7C10 VH</b>	FPGNKLEWMG <b>YISYDGTNNYKPSLKD</b> RISITRDTSKNQFFL
<b>AN03' CL</b>	..... <b>..N...N...N...N</b> .....
Kabat sgI(A)	..... <b>...S.STY.N...S</b> ..... <u>Y</u> ..

	84	<b>CDR 3</b>
<b>7C10 VH</b>	KLNSVTNEDTATYYCAR <b>YGRV-FFDY</b> WGQGTTLTVSS	
<b>AN03' CL</b>	..... <u>T</u> ..... <b>E.YGY</b> .....	
Kabat sgI(A)	<u>Q</u> ..... <u>T</u> ..... <b>G.YGYG</b> ..... <u>V</u> .....	

FIGURE 22

	<b>Rch 1</b>	30	<b>CDR 1</b>	<b>Rch 2</b>
7C10 VH mouse	DVQLQESGPGGLVKPSQSLSLTCSVTGYSIT		<b>GGYLWN</b>	WIRQ
human Kabat sgII	Q.....T.....T.S. <u>G</u> . <u>V</u> S		<b>SYWS</b> ..	....
human VH FUR1'CL	Q.....ET.....T.S....S		<b>S..Y.S</b>	....
human Germline	Q.....ET.....T.S....S		<b>S..Y.S</b>	....

	<b>Rch 2</b>	48	<b>CDR 2</b>	67	71	<b>Rch 3</b>
7C10 VH mouse	FPGNKLEWMG <b>YISYDGTNNYKPSLKD</b>		RISITRDTSKNQFFL			
human Kabat sgII	P..KG...I. <b>R.Y.S.STX.N....S</b>		.VT. <u>S</u> <u>V</u> .....S.			
human VH FUR1'CL	P..KG...I. <b>SMFHS.SSY.N....S</b>		.VT. <u>S</u> <u>V</u> .....S.			
human Germ-line	P..KG...I. <b>S.YHS.STY.N....S</b>		.VT. <u>S</u> <u>V</u> .....S.			

	<b>Rch 3</b>	<b>CDR 3</b>	<b>Rch 4</b>
7C10 VH mouse	KLNSVTNEDTATYYCAR <b>YGRVFFDY</b>		WGQGTTLTVSS
human Kabat sgII	..S...AA...V..... <b>ELPGGYDV</b>		.....LV....
human VH FUR1'CL	<b>Q.R...AA...V.....</b> <b>GRYCSSTSCNWFD</b>		.....LV....
human Germline	..S...AA...V.....		

FIGURE 23



		30	CDR 1	48
7C10 VH mouse	DVQLQESGPGLVKPSQSLTCSVTGYSIT	<u>GGYLWN</u>	WIRQFPGNKLEW	<u>MG</u>
human germline	Q.....ET.....T.S....	<u>S</u> S..Y.G	....P..KG...	<u>I</u> .
VH Humanized 1	Q.....ET.....T.S....		....P..KG....	
VH Humanized 2	Q.....ET.....T.S....		....P..KG...	<u>I</u> .
VH Humanized 3	Q.....ET.....T.S....	<u>S</u>	....P..KG...	<u>I</u> .

	CDR 2	67	71
7C10 VH mouse	<u>YISYDGTNNYKPSLKD</u>	RISITR	DTSKNQFFLKLNSVTNEDTATYYCAR
human germline	S.FHS.SSY.N....S	<u>VT</u> . <u>SV</u> .....	S...S...AA...V.....
VH Humanized 1		.T.S.....	S...S...AA...V.....
VH Humanized 2		<u>VT</u> .S.....	S...S...AA...V.....
VH Humanized 3		<u>VT</u> . <u>SV</u> .....	S...S...AA...V.....

	CDR 3
7C10 VH mouse	<u>YGRVFFDY</u> WGQGTTLTVSS
human germline	
VH Humanized 1	.....LV....
VH Humanized 2	.....LV....
VH Humanized 3	.....LV....

FIGURE 24

MluI

```

      |
GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT
1  -----+-----+-----+-----+-----+-----+-----+ 60
CAGTCTTGCGCACGGCGGTGGTACTTTTACAACCTCAGACAACATGGAGAACTGTCGGTAA

      M K V L S L L Y L L T A I -
      Leader peptide
CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCG
61 -----+-----+-----+-----+-----+-----+-----+ 120
GGACCATAGGACAGAGTCCACGTCTGAAGTCCTCAGCCCGGGTCCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -
GAGACCCTGTCCCTCACCTGCACTGTCTCTGGTTACTCCATCACCGGTGGTTATTTATGG
121 -----+-----+-----+-----+-----+-----+-----+ 180
CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTGGCCACCAATAAATACC

      30          CDR 1
E T L S L T C T V S G Y S I T G G Y L W -
AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATGGGGTATATCAGCTACGAC
181 -----+-----+-----+-----+-----+-----+-----+ 240
TTGACCTATGCCGTCGGGGGTCCCTTCCCTGACCTCACCTACCCCATATAGTCGATGCTG

      48
N W I R Q P P G K G L E W M G Y I S Y D -
      KpnI
      |
GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAATCACCATATCACGTGACACGTCC
241 -----+-----+-----+-----+-----+-----+-----+ 300
CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTTAGTGGTATAGTGCACCTGTGCAGG

      CDR 2          67          71
G T N N Y K P S L K D R I T I S R D T S -
AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
301 -----+-----+-----+-----+-----+-----+-----+ 360
TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTCACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -
TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCCTGGTCACCGTC
361 -----+-----+-----+-----+-----+-----+-----+ 420
ACACGCTCTATGCCATCCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCAGTGGCAG

      CDR 3
C A R Y G R V F F D Y W G Q G T L V T V -

      BamHI
      |
TCCTCAGGTGAGTGGATCCTCTGCG
421 -----+-----+-----+-----+-----+-----+-----+ 445
AGGAGTCCACTCACCTAGGAGACGC

S S -
  
```

FIGURE 25

MluI  
 |  
 GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT  
 1 -----+-----+-----+-----+-----+-----+ 60  
 CAGTCTTGCGCACGGCGGTGGTACTTTCACAACCTCAGACAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -  
 Leader peptide

CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG  
 61 -----+-----+-----+-----+-----+-----+ 120  
 GGACCATAGGACAGAGTCCACGTCTGAAGTCCTCAGCCCCGGGTCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -

GAGACCCTGTCCCTCACCTGCAGTGTCTCTGGTTACTCCATCACCGGTGGTTATTTATGG  
 121 -----+-----+-----+-----+-----+-----+ 180  
 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAAATACC

30 CDR 1

E T L S L T C T V S G Y S I T G G Y L W -

AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC  
 181 -----+-----+-----+-----+-----+-----+ 240  
 TTGACCTATGCCGTGCGGGGTCCCTTCCCTGACCTACCTAGCCCATATAGTCGATGCTG

48

N W I R Q P P G K G L E W I G Y I S Y D -

KpnI  
 |  
 GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAGTCACCATATCACGTGACACGTCC  
 241 -----+-----+-----+-----+-----+-----+ 300  
 CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTCAGTGGTATAGTGCACTGTGCAGG

CDR 2 67 71

G T N N Y K P S L K D R V T I S R D T S -

AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC  
 301 -----+-----+-----+-----+-----+-----+ 360  
 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -

TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCTGGTACCGTC  
 361 -----+-----+-----+-----+-----+-----+ 420  
 ACACGCTCTATGCCATCCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCAGTGGCAG

CDR 3

C A R Y G R V F F D Y W G Q G T L V T V -

BamHI  
 |  
 TCCTCAGGTGAGTGGATCCTCTGCG  
 421 -----+-----+-----+-----+ 445  
 AGGAGTCCACTCACCTAGGAGACGC

S S -

FIGURE 26

MluI  
 |  
 GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT  
 1 -----+-----+-----+-----+-----+-----+ 60  
 CAGTCTTGCGCACGGCGGTGGTACTTTTCACTCAGACAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -  
 Leader peptide  
 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG  
 61 -----+-----+-----+-----+-----+-----+ 120  
 GGACCATAGGACAGAGTCCACGTCAAGTCCTCAGCCCCGGTCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -  
 GAGACCCTGTCCCTCACCTGCACTGTCTCTGGTTACTCCATCAGCGGTGGTTATTTATGG  
 121 -----+-----+-----+-----+-----+-----+ 180  
 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAAATACC

30 CDR 1  
 E T L S L T C T V S G Y S I S G G Y L W -  
 AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC  
 181 -----+-----+-----+-----+-----+-----+ 240  
 TTGACCTATGCCGTCGGGGTCCCTTCCCTGACCTACCTAGCCCATATAGTCGATGCTG

48  
N W I R Q P P G K G L E W I G Y I S Y D -  
 KpnI  
 |  
 GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAGTCACCATATCAGTGGACACGTCC  
 241 -----+-----+-----+-----+-----+-----+ 300  
 CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTCAGTGGTATAGTCACCTGTGCAGG

CDR 2 67 71  
 G T N N Y K P S L K D R V T I S V D T S -  
 AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC  
 301 -----+-----+-----+-----+-----+-----+ 360  
 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -  
 TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC  
 361 -----+-----+-----+-----+-----+-----+ 420  
 ACACGCTCTATGCCATCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCACTGGCAG

CDR 3  
 C A R Y G R V F F D Y W G Q G T L V T V -  
 BamHI  
 |  
 TCCTCAGGTGAGTGGATCCTCTGCG  
 421 -----+-----+-----+-----+-----+ 445  
 AGGAGTCCACTCACCTAGGAGACGC

S S

FIGURE 27

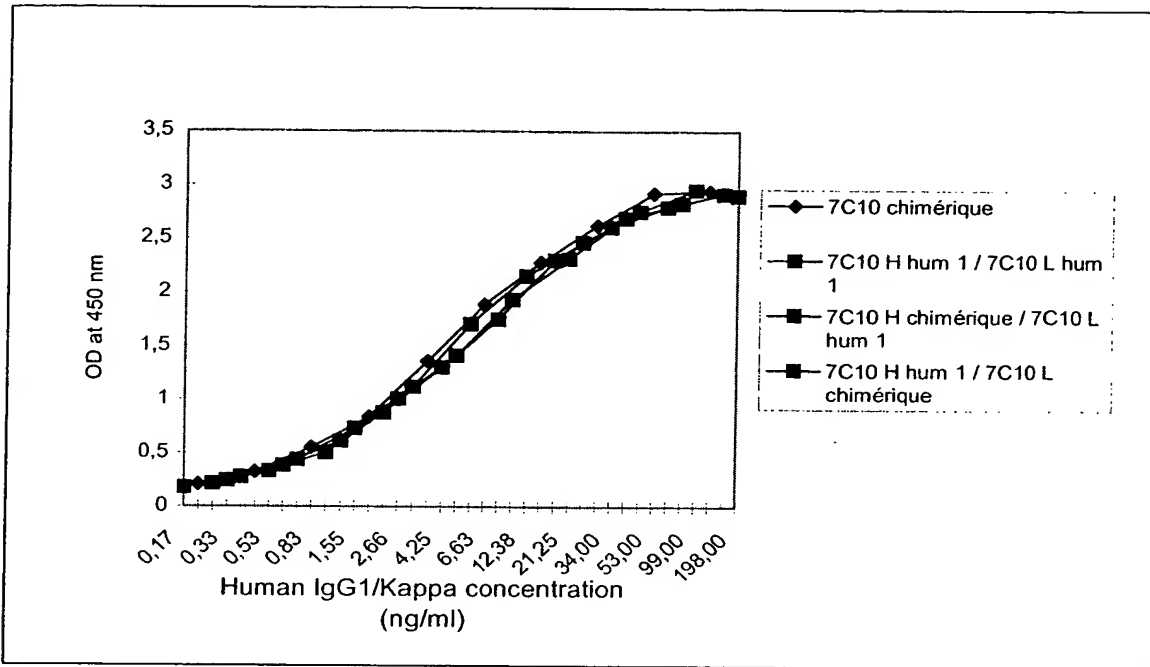


FIGURE 28

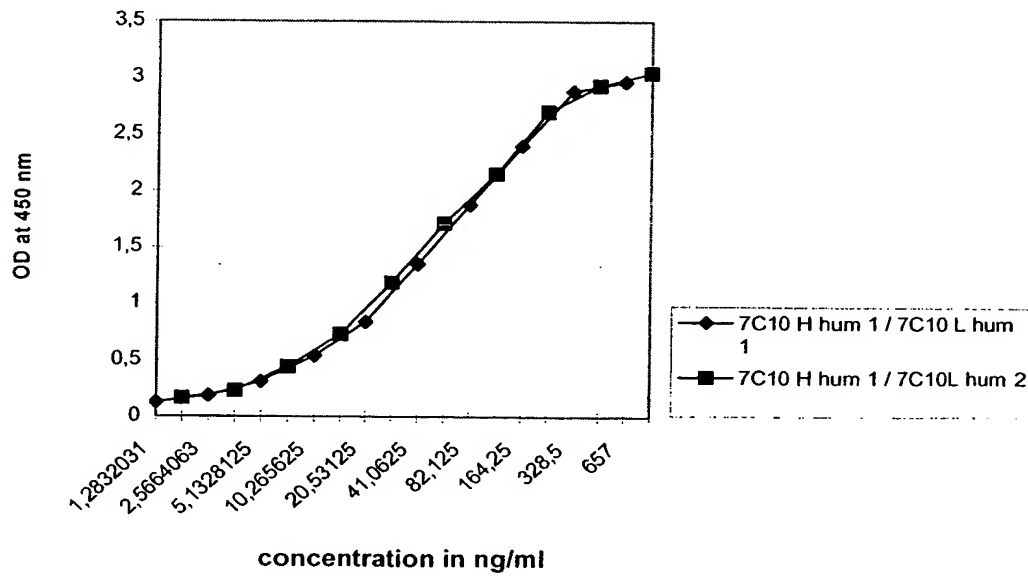


FIGURE 29

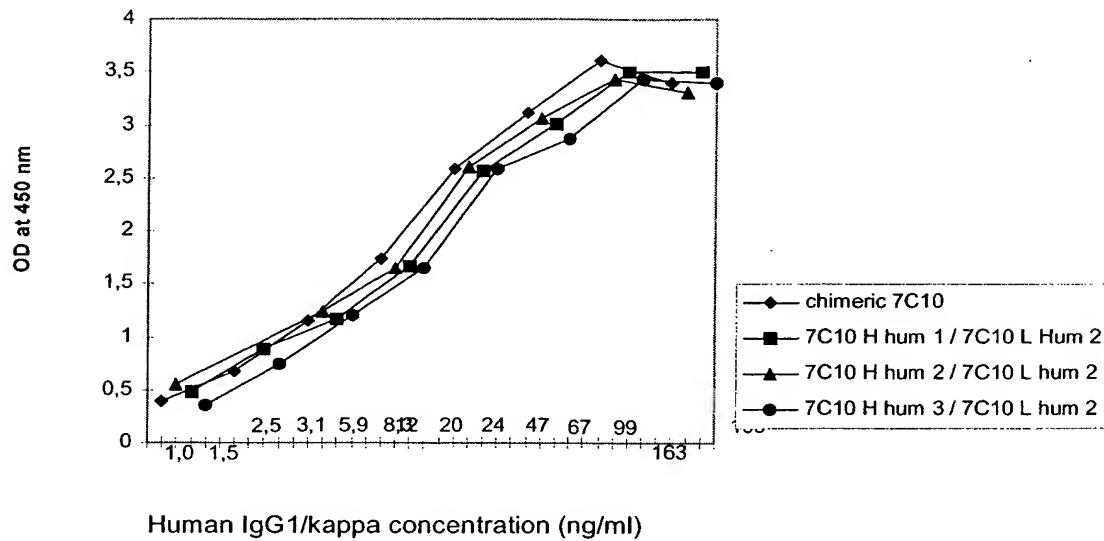


FIGURE 30

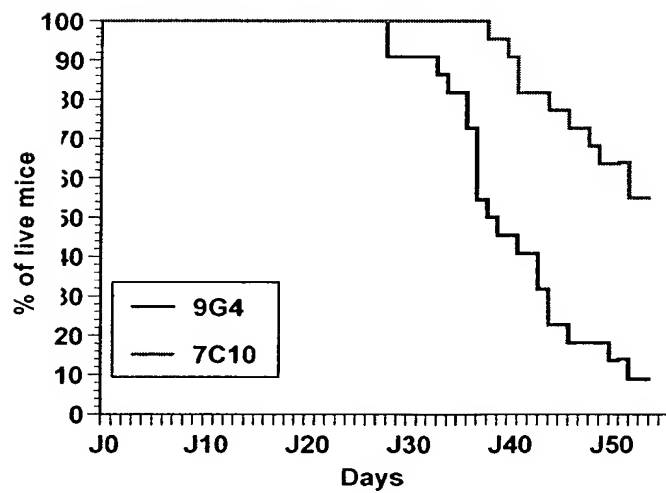
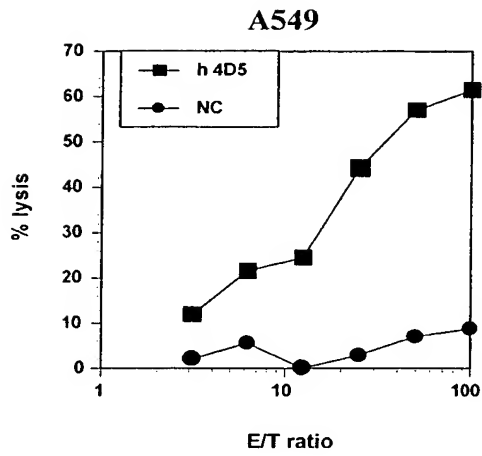
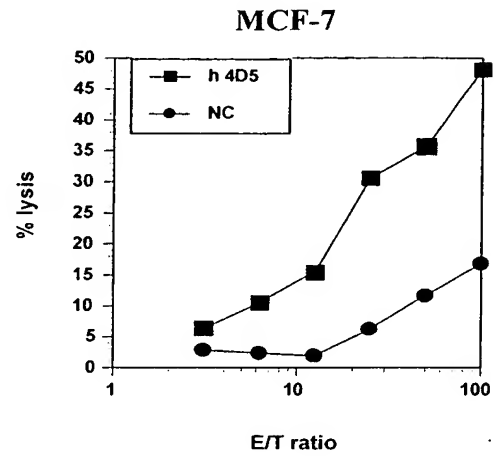


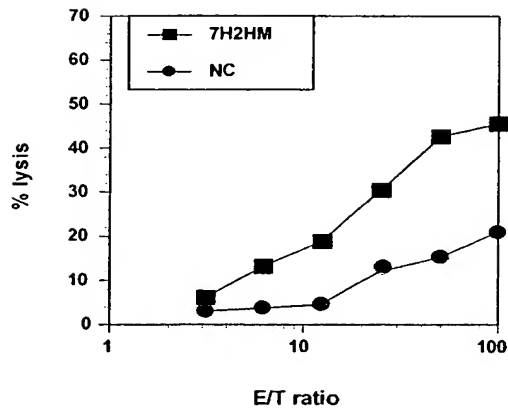
FIGURE 31



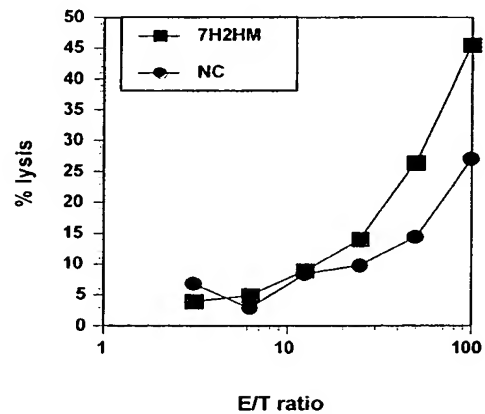
**FIGURE 32A**



**FIGURE 32B**



**FIGURE 32C**



**FIGURE 32D**

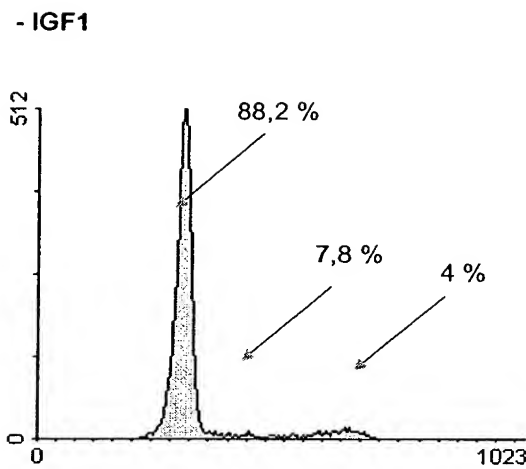


FIGURE 33A

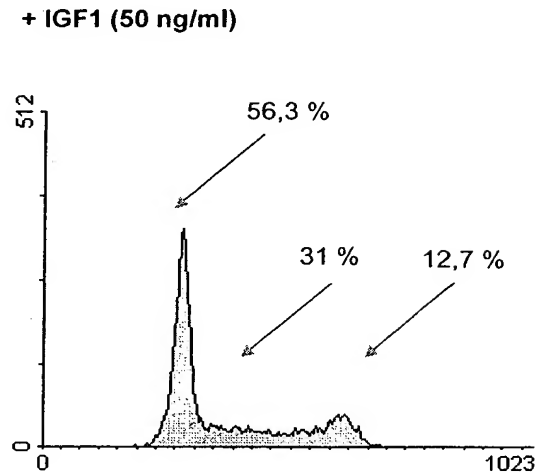


FIGURE 33B

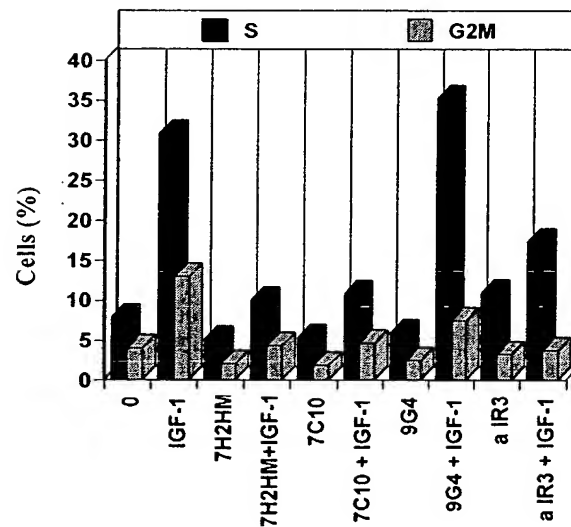


FIGURE 33C



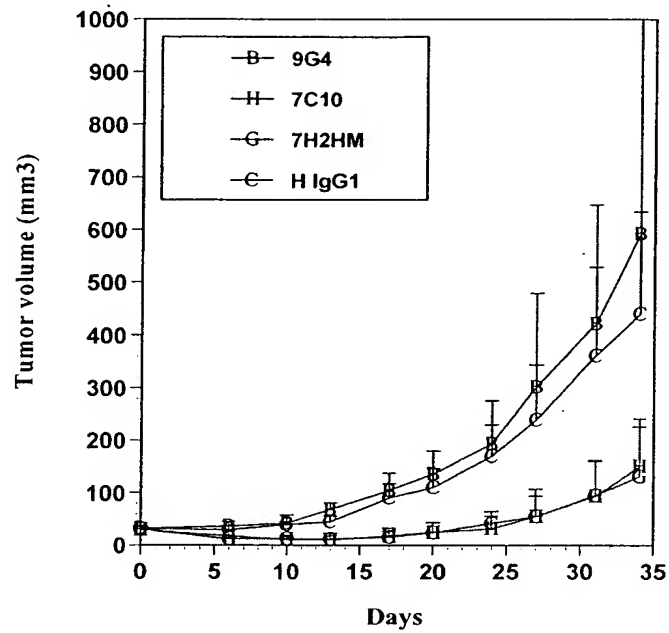


FIGURE 34A

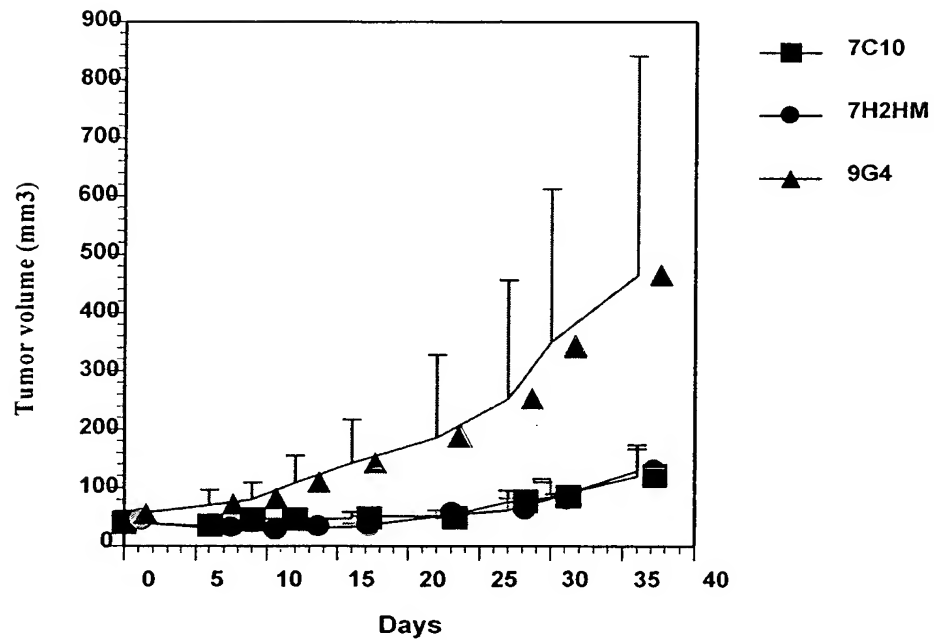


FIGURE 34B

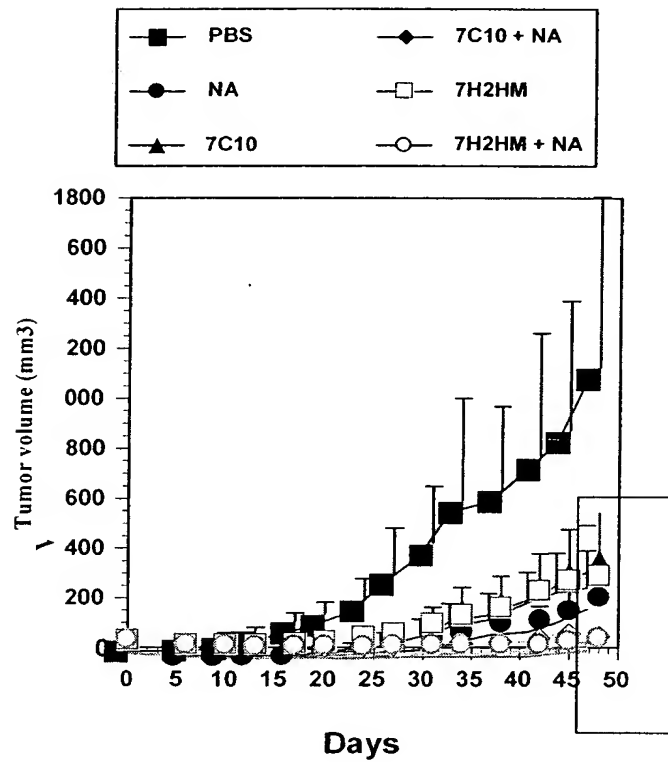


FIGURE 35A

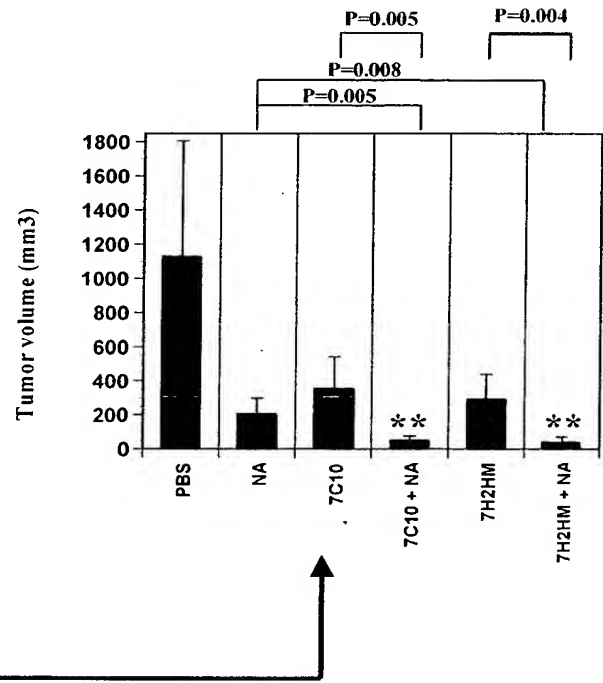


FIGURE 35B

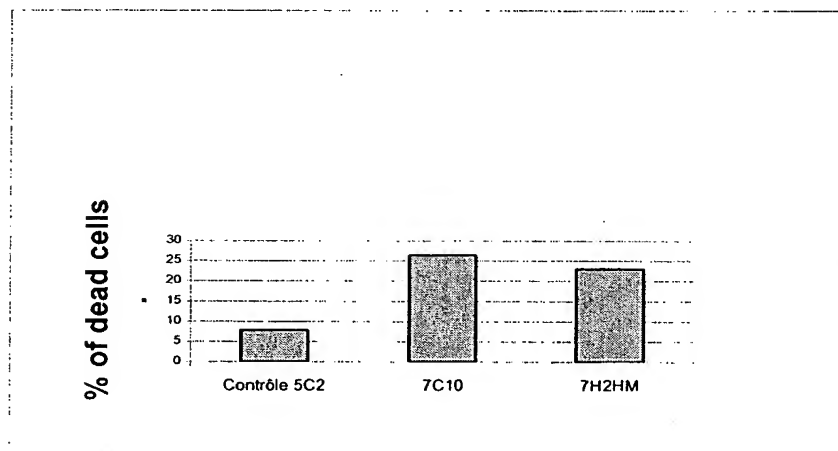


FIGURE 36

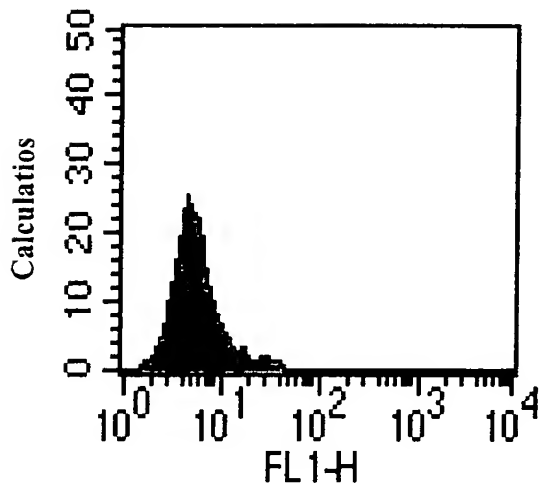


FIGURE 37A

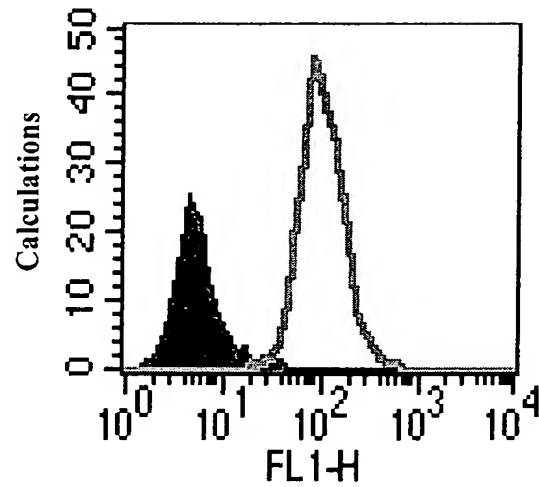


FIGURE 37B

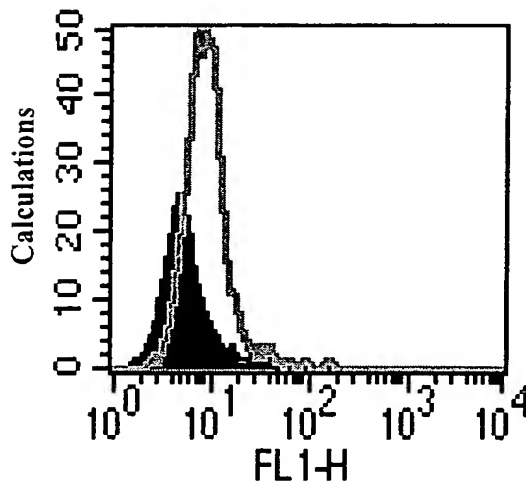


FIGURE 37C

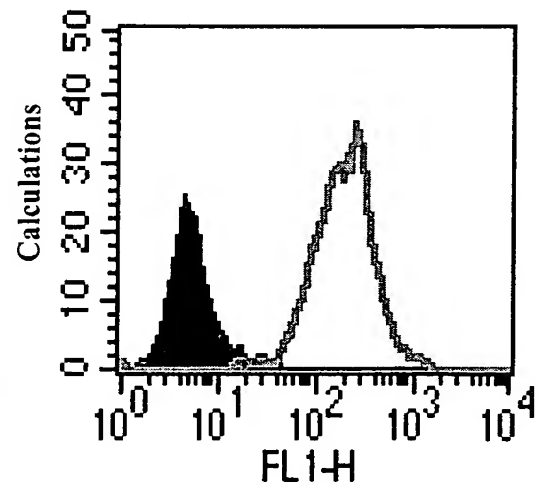


FIGURE 37D

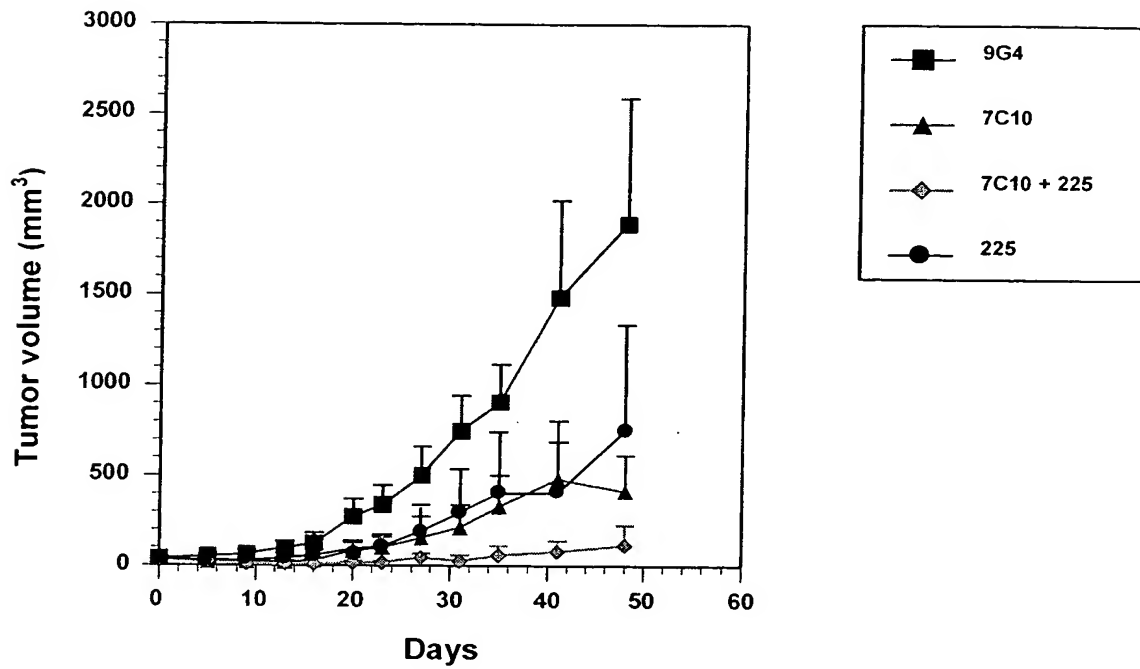


FIGURE 38

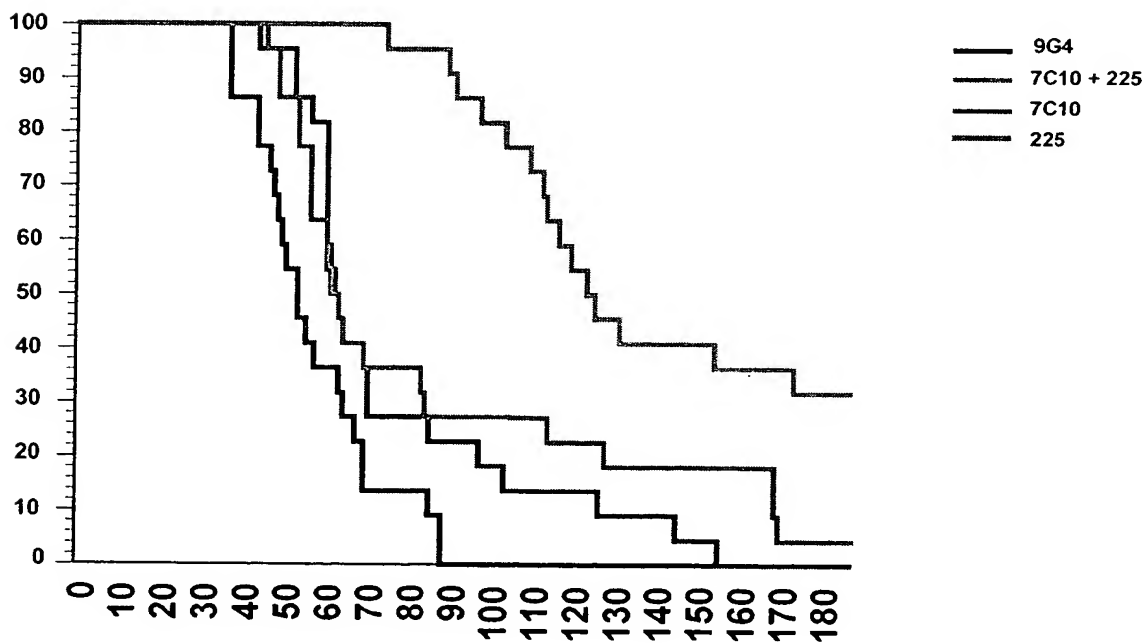


FIGURE 39

FIGURE 40A

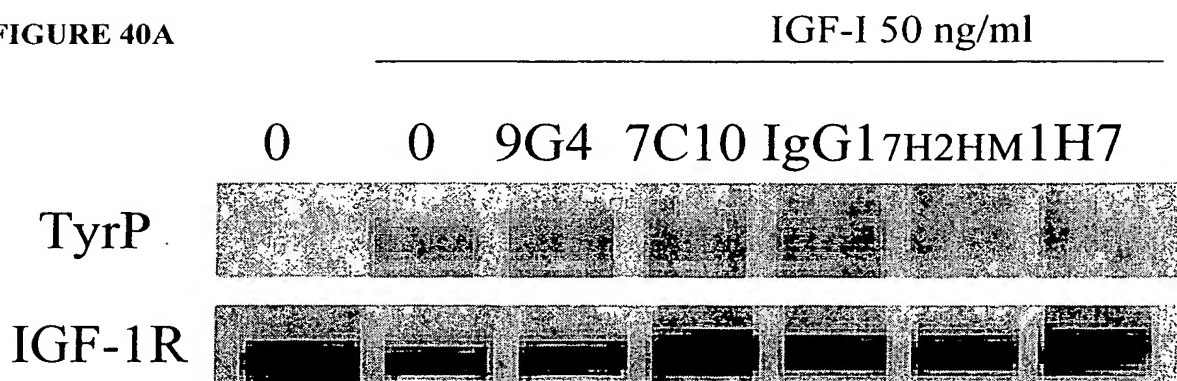


FIGURE 40B

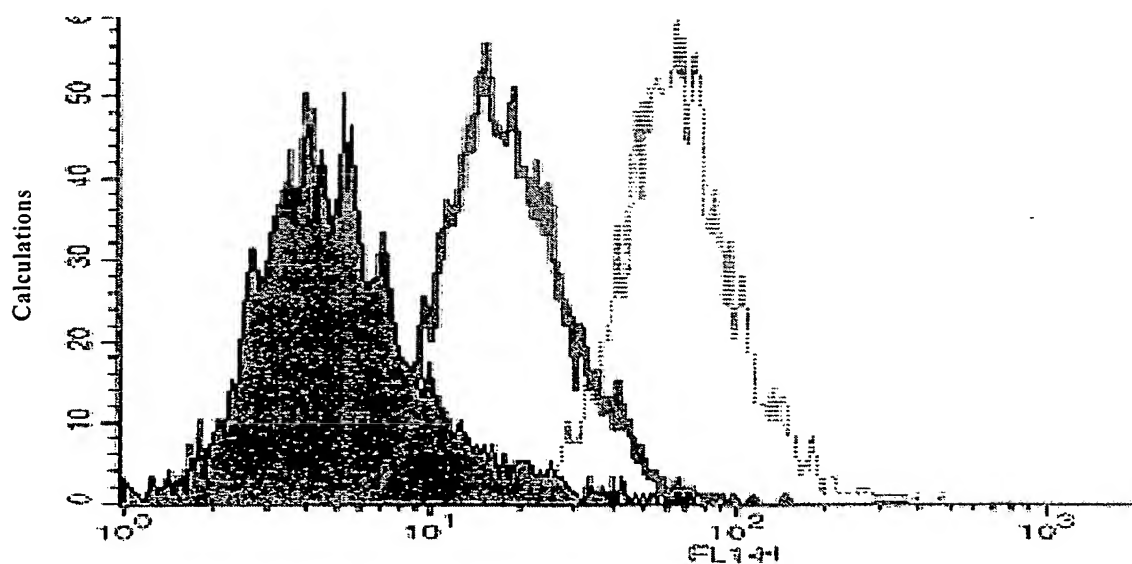
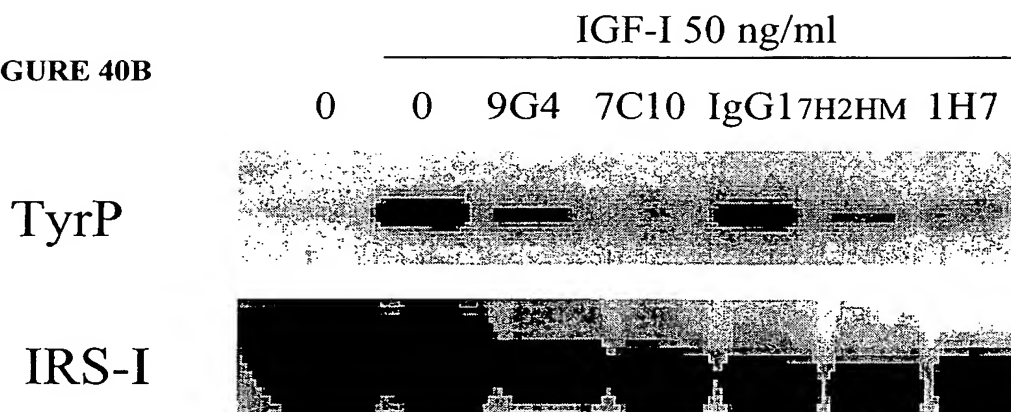


FIGURE 41

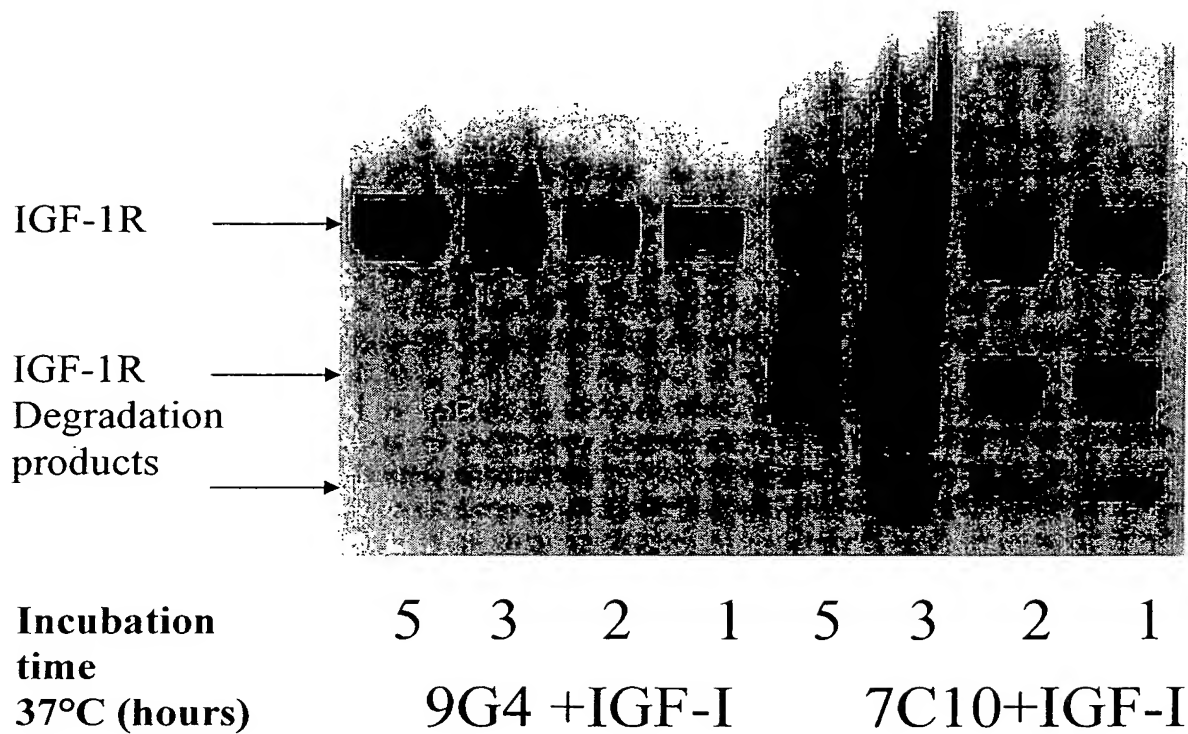


FIGURE 42A

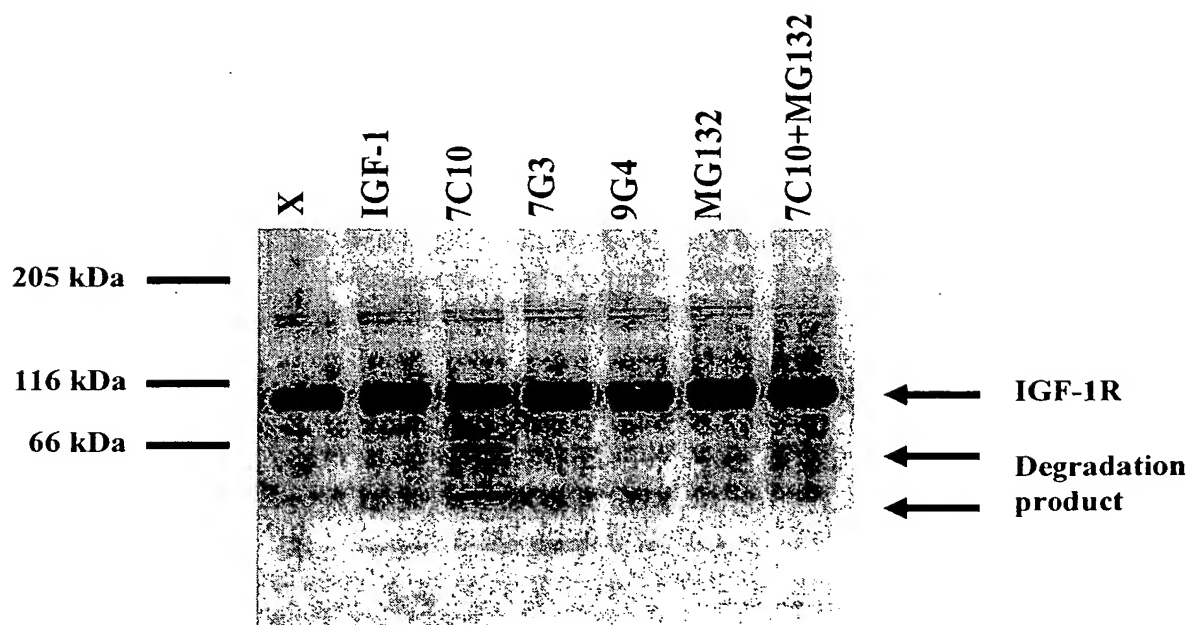


FIGURE 42B

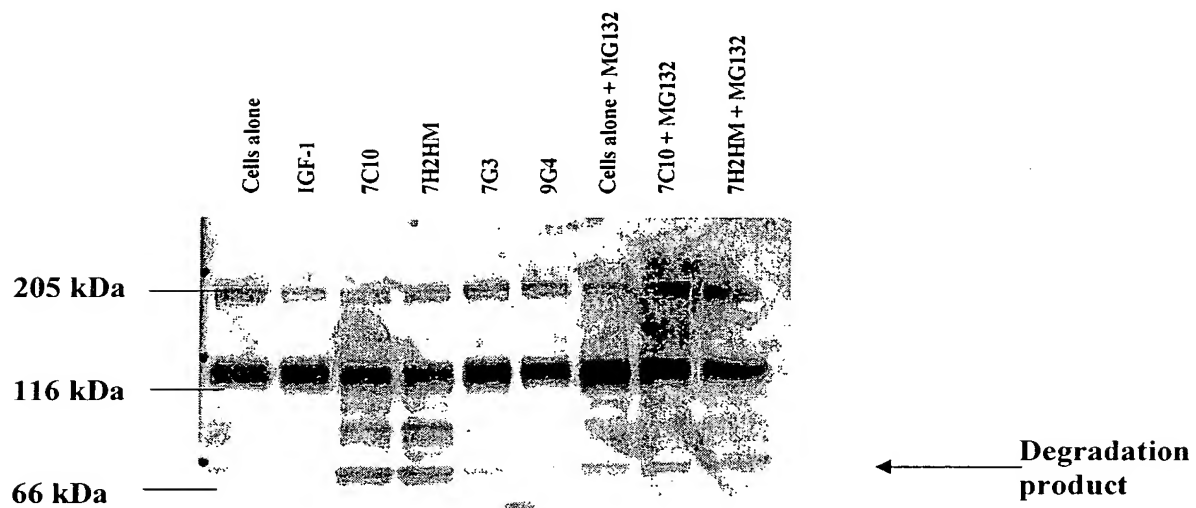


FIGURE 42C

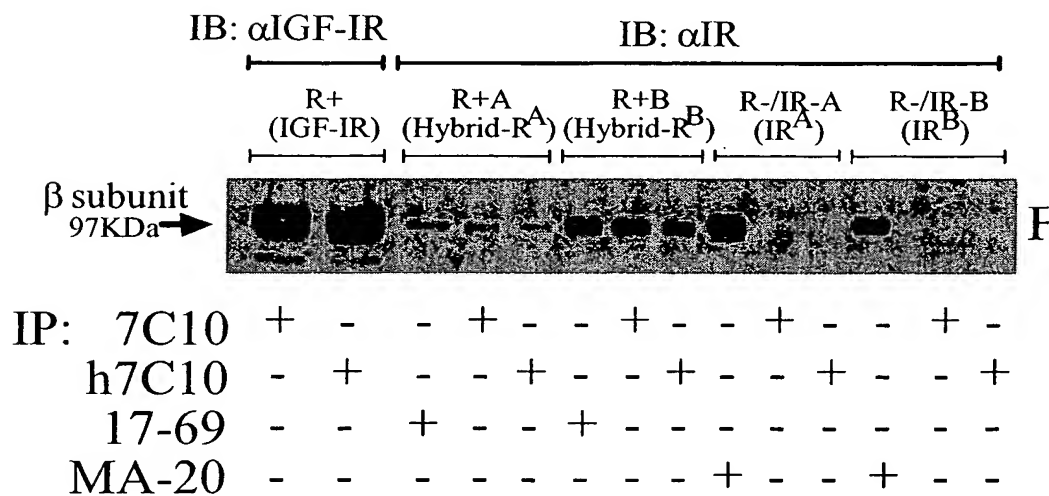


FIGURE 43A

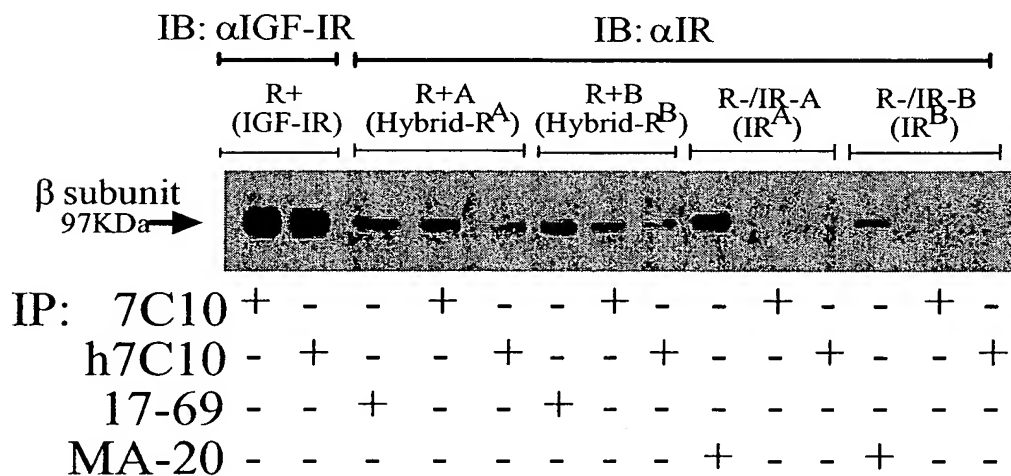


FIGURE 43B



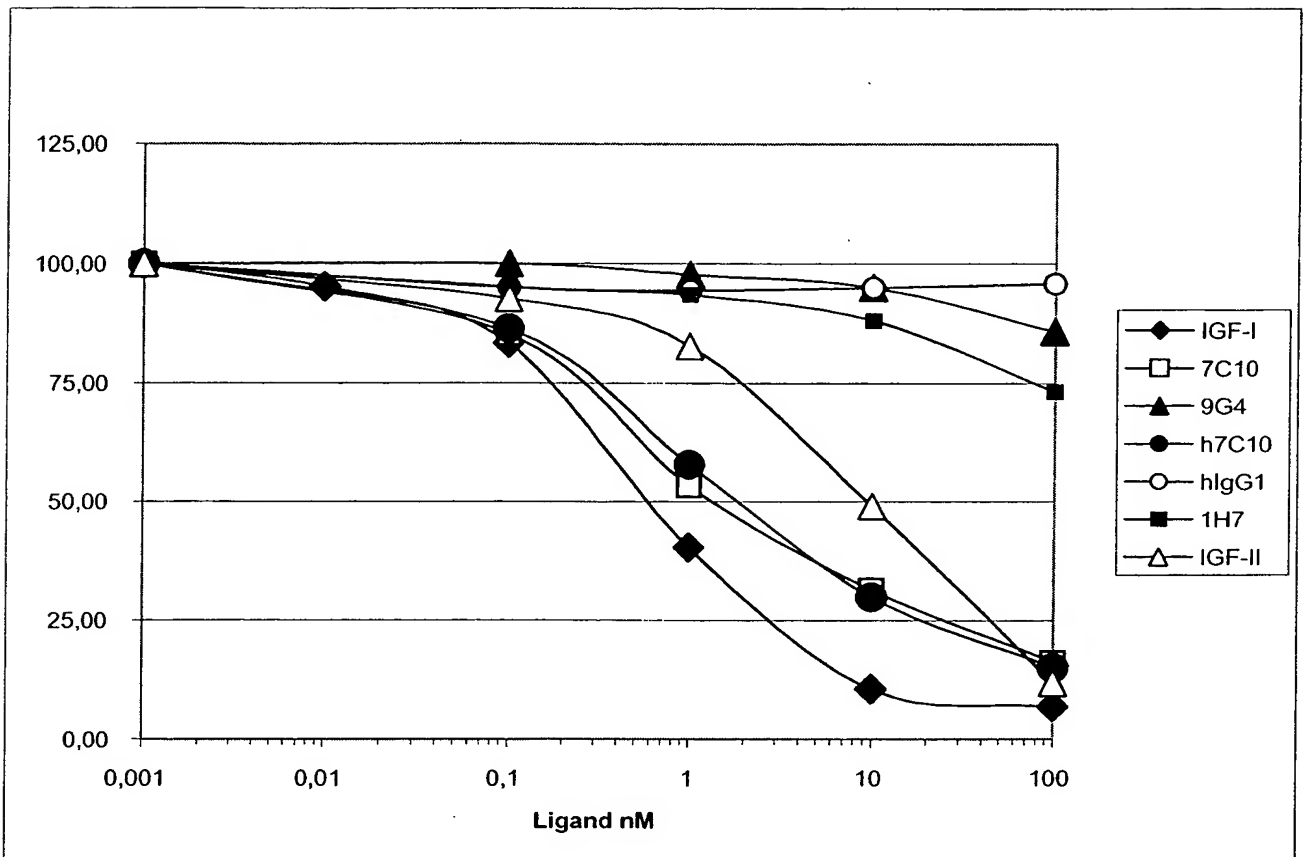


FIGURE 44

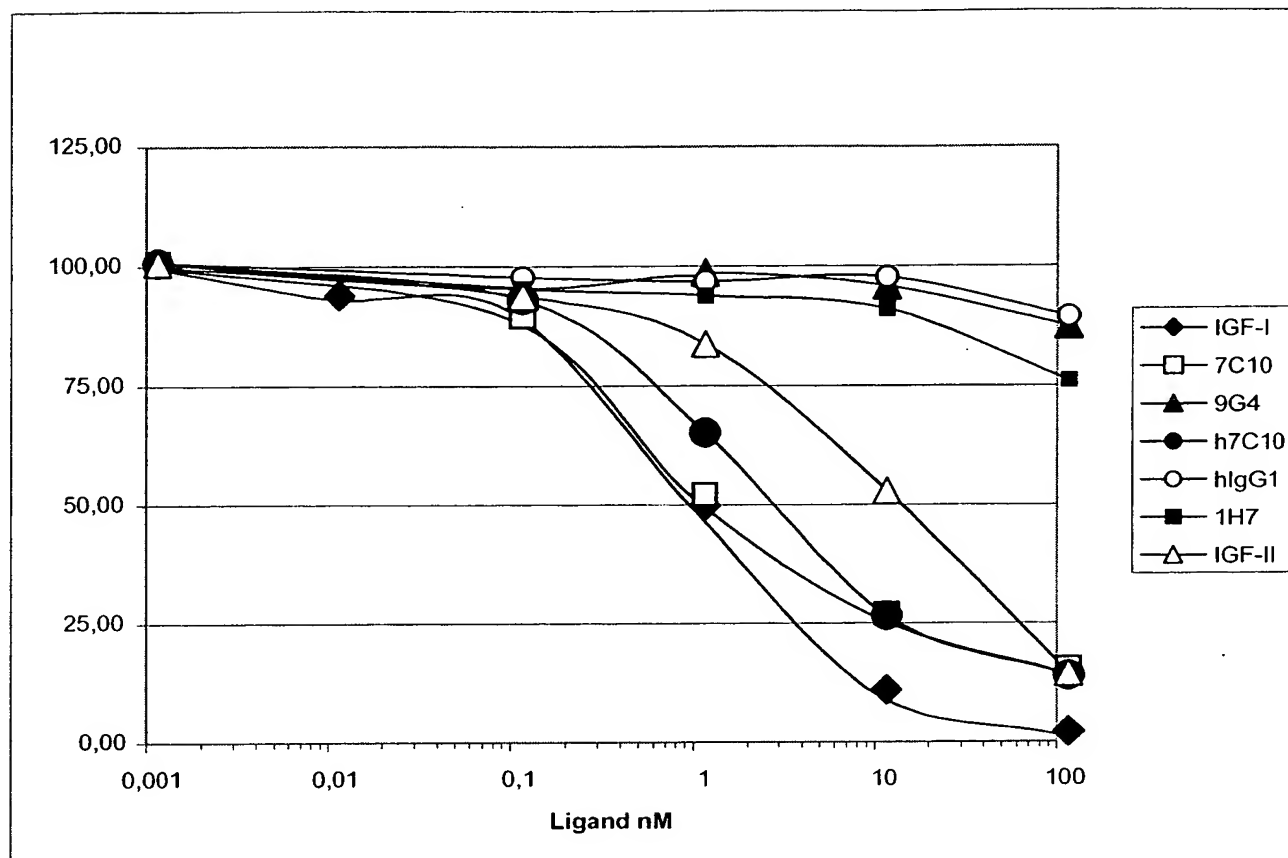


FIGURE 45

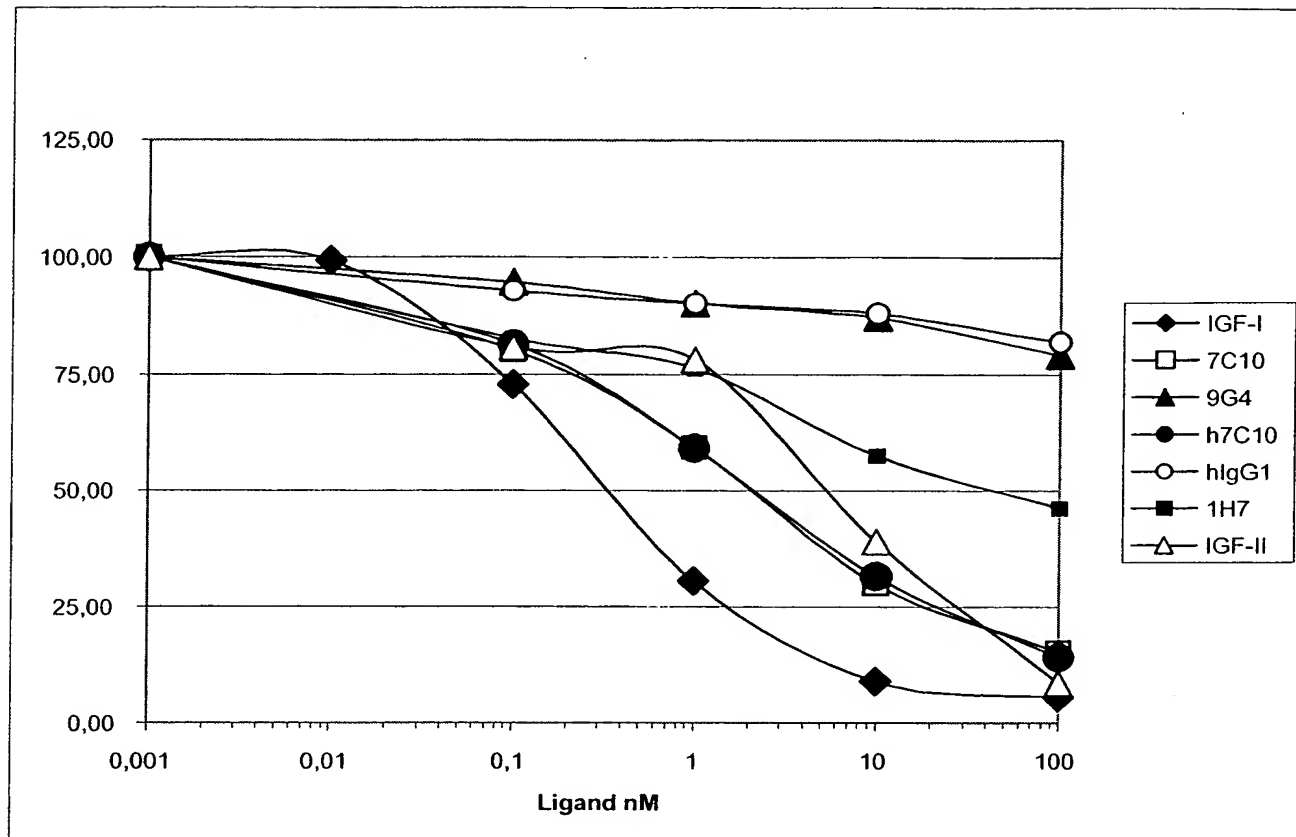


FIGURE 46



FIGURE 47A

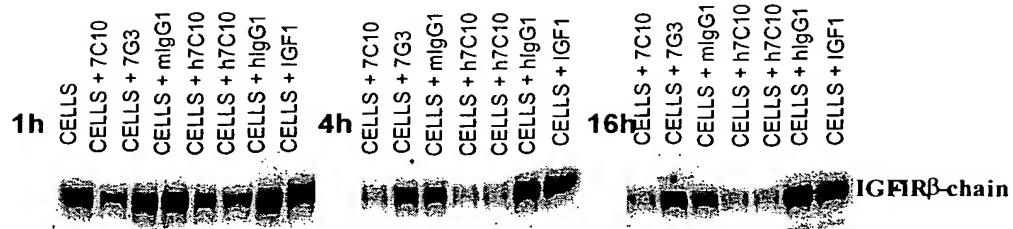


FIGURE 47B

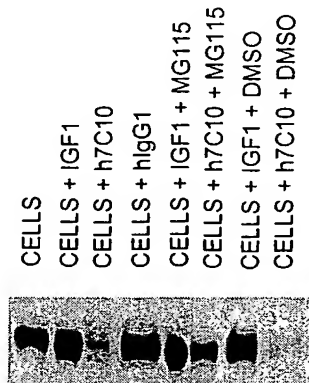


FIGURE 48

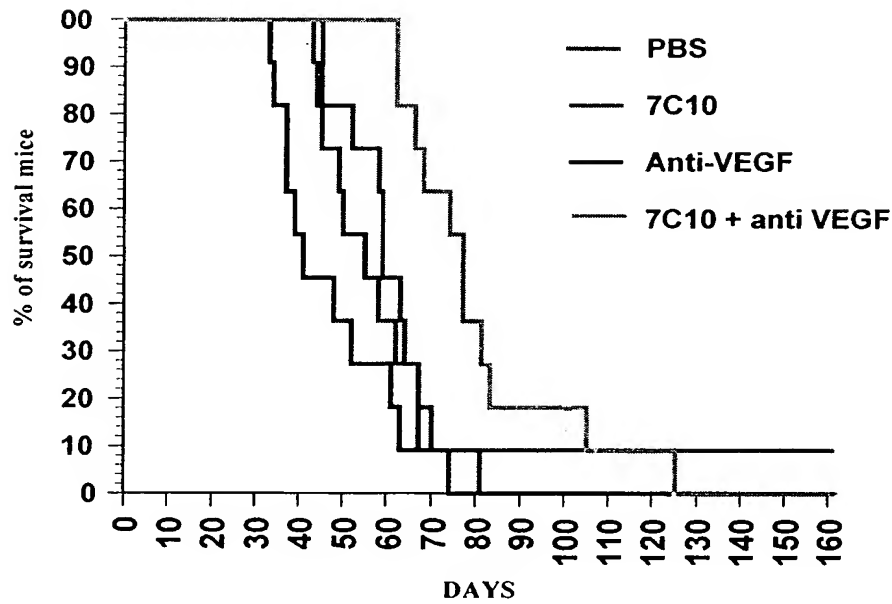


FIGURE 49

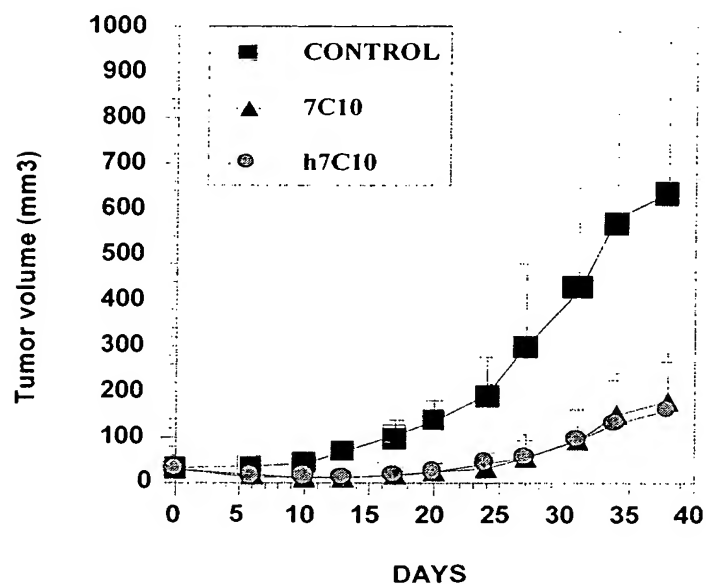


FIGURE 50

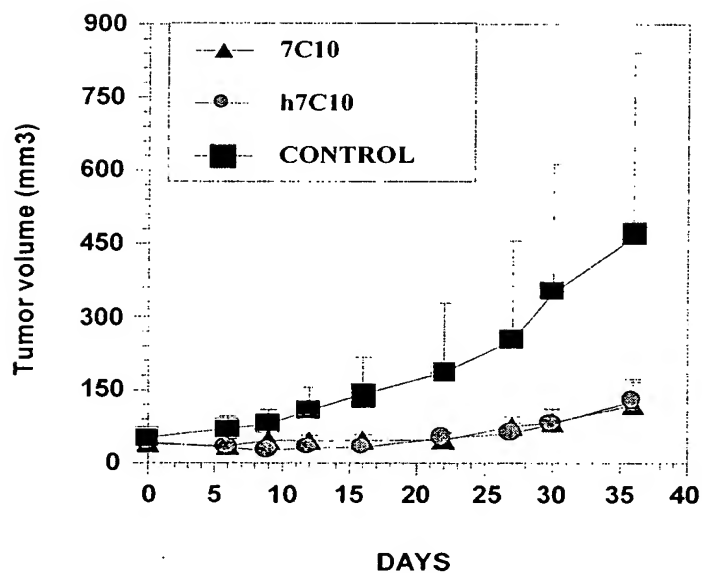


FIGURE 51

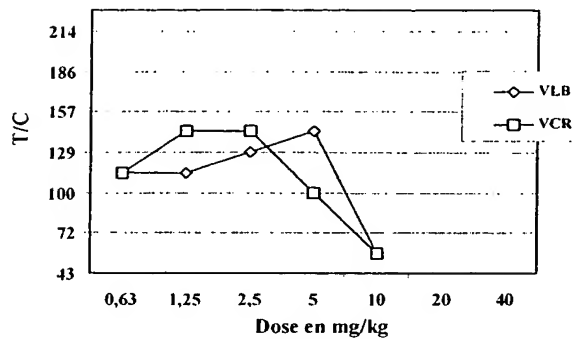


FIGURE 52

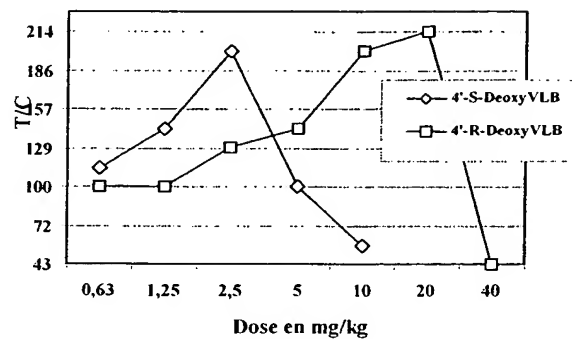


FIGURE 53

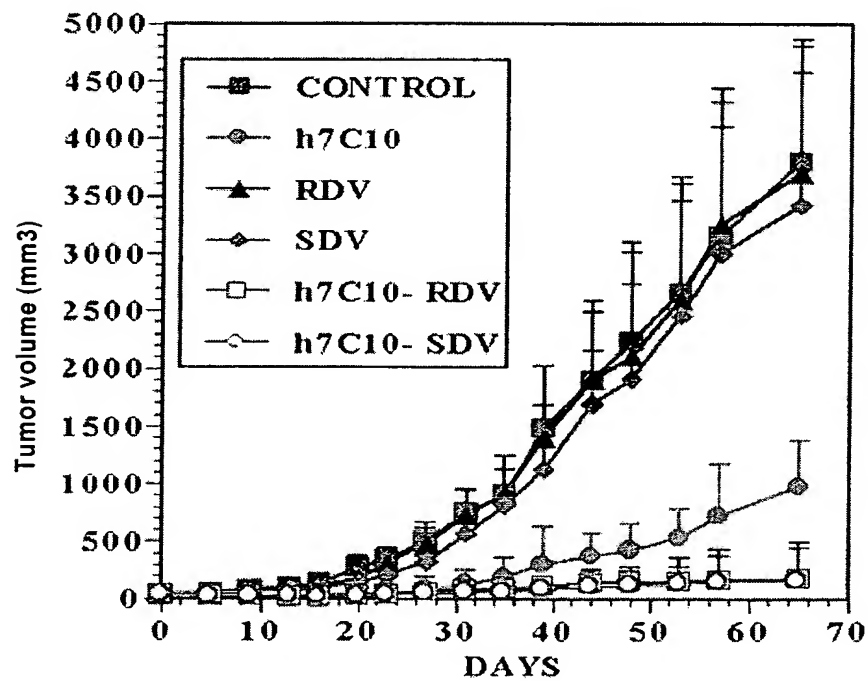


FIGURE 54

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**